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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,797	12/04/2001	John David Fraser	12669-002001/30072UPS00	9884
69713 7590 08/27/2007 OCCHIUTI ROHLICEK & TSAO, LLP 10 FAWCETT STREET CAMBRIDGE, MA 02138			EXAMINER JUEDES, AMY E	
			ART UNIT 1644	PAPER NUMBER
			MAIL DATE 08/27/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/006,797

Applicant(s)

FRASER ET AL.

Examiner

Amy E. Juedes, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-11, 13-18 and 21-39 is/are pending in the application.
- 4a) Of the above claim(s) 7-9, 14, 17, 18 and 21-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-6, 10, 11, 13, 15, 16 and 39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 6/22/07 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 6/22/07 and 4/24/07 has been entered.

Claims 2-6, 10-11, 13, 15-16, and 39 have been amended.
Claims 2-11, 13-18, and 21-39 are pending.

Claims 7-9, 14, 17-18, and 21-38 stand withdrawn from further consideration pursuant to 37 CFR 1.14209 as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 2-6, 10-11, 13, 15-16, and 39 are under examination.

2. The rejection of the claims under 35 U.S.C. 112 second paragraph is withdrawn in view of Applicant's amendment to remove the term "immunomodulator" from the claims.

3. The rejection of the claims under 35 U.S.C. 102 as being anticipated by Yamaoka et al. is withdrawn in view of Applicant's amendment to recite that the conjugate binds to MHC class II, and submission of evidentiary data demonstrating that conjugation of peptides to the N-terminus of SPE-C prevents MHC class II binding.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5, 11, 13, 15-16, and 39 stand rejected, and claims 6 and 10 are rejected, under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art

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that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) An immunomodulator comprising a targeting molecule that "includes a Class II MHC binding site" and a T cell receptor binding site of a superantigen, the T binding site having one or more mutations that "reduce its T cell proliferation activity"

B) An immunomodulator wherein the mutated T cell receptor binding site "reduces the T cell proliferation activity to equal to or greater than 10,000 fold"

Applicant indicates that support for the limitations of claim 2 can be found on page 3 of the specification, and support for new claim 39 can be found in Table 3 at page 21 of the specification.

A review of the specification fails to reveal support for the new limitation.

Regarding A), the instant specification discloses on pg. 3 a targeting molecule that mimics a superantigen but does not include a fully functional T-cell receptor binding site and a targeting molecule which is structurally a superantigen but for a disrupted T-cell receptor binding site. However, there is no disclosure of a targeting molecule that specifically "includes a class II binding site", as now claimed. Furthermore, the targeting molecules disclosed on page 3 include those without a fully functional T cell receptor binding site, or those that have little or no ability to activate T cells. However, these generic disclosures are not adequate to support claims which specifically recite that the T cell binding site "reduces T cell proliferation activity".

Regarding B), the instant specification on page 21 discloses specific targeting molecules such as SMEZ-2 W75L that reduce T cell proliferation to greater than 10,000 fold. However, this specific example is not adequate to support the more generic claims of the instant application which are drawn to an immunomodulator comprising any superantigen with any mutation in the T cell binding site.

Applicant's arguments filed 4/24/07 have been fully considered, but they are not persuasive.

Regarding A), Applicant argues all superantigens contain a Class II MHC binding site, and that the skilled artisan would understand that the disclosure of a molecule which is structurally a superantigen but for a disrupted T cell receptor binding site would include a MHC class II binding site.

The instant specification discloses a molecule that is structurally a superantigen, but for a disrupted T cell receptor binding site. However, this does not have the same scope as claims drawn to a molecule that "includes a Class II MHC binding site" of a superantigen. For example, a molecule that is "structurally a superantigen" might include proteins that exhibit a high degree of homology to a superantigen, but would

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not necessarily require a MHC class II binding site, as recited in the instant claims.

Applicant further argues that the specification discloses molecules with disrupted T cell receptor binding sites such that the molecule have little or no ability to activate T cells. Applicant states that the specification further discloses on page 15 that the loss of T cell activity can be T cell proliferation.

Page 15 of the specification discloses a specific example of testing SPE-C mutants utilizing in vitro T cell proliferation assays. This does not provide adequate support for the instant claims which broadly encompass any molecule comprising a MHC II binding site of a superantigen and a T cell binding site with one or more mutations that "reduce its T cell proliferation activity".

Regarding B), Applicant argues that the specific mutants disclosed by the specification that reduce T cell proliferation greater than 10,000 fold constitute a representative number of species within the claimed genus to demonstrate that Applicant was in possession of the invention.

Newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure (see MPEP 2163 section IB), and not by a "representative" number of species.

5. The following are new grounds of rejection.

6. Claims 5-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of targeting molecules "derived from" *Staphylococcus aureus* and/or *Streptococcus pyogenes*.

The instant claims are drawn to a conjugate comprising a targeting molecule that includes a Class II binding site of a superantigen, wherein the targeting molecule is "derived from" *Staphylococcus aureus* and/or *Streptococcus pyogenes*. Thus, the

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claims might encompass structurally different targeting molecules that have been "derived from" any protein expressed in *Staphylococcus aureus* or *Streptococcus pyogenes*. The only requirement is that the targeting molecule comprise a Class II binding site. However, given enough amino acid substitutions, additions, or deletions, a protein comprising a class II binding site can be "derived from" any another protein. Additionally, the claims might encompass superantigen "derivatives" comprising other types of chemical modifications. In contrast to the broad genes of structurally different targeting molecules encompassed by the claims, the instant specification only discloses targeting molecules that comprise a superantigen of *Staphylococcus aureus* or *Streptococcus pyogenes* (for example, SPEC), wherein the superantigen comprises a mutated T cell receptor binding site. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

7. Claims 2-6, 10-11, 13, 15-16, and 39 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A conjugate the "binds to a Class II MHC molecule" (Claim 2, and dependant claims 3-6, 10-11, 13, 15-16, and 39).

Applicant indicates that support for the new limitations of the claims can be found on page 15 and 22 of the specification.

A review of the specification fails to reveal support for the new limitations.

At page 22, the specification discloses a specific example of testing in vivo T cell response to a particular superantigen construct. However, there is no disclosure of a conjugate that "binds to a Class II MHC molecule". Page 15 of the

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specification discloses a specific example of generating specific SPEC mutants and testing the mutants for their ability to bind to MHC class II. However, the disclosure of a specific example of testing mutants of SPEC for their ability to bind MHC does not provide adequate support for superantigen "conjugates" that bind to MHC, as now claimed.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 2-6, 10-11, 13, 15-16, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCormick et al., 2000, in view of U.S. Patent 5,116,964.

McCormick et al. teach a vaccine for inducing a protective immune response in vivo comprising SPEC that has been mutated at residues 15 and 38 (see page 308 in particular). McCormick et al. teach that the mutations to SPEC abolish its ability to stimulate T cell proliferation, reducing proliferation to background levels (i.e. more than 10,000 fold, see figure 3 and 4 in particular). Thus, the T cell binding site of the superantigen has been deleted (i.e. is nonfunctional). Furthermore, since the instant specification teaches on pages 19-20 that residues 22-90 of SPEC are not involved in MHC binding, the superantigen taught by McCormick comprising mutations at residues 15 and 38 would inherently maintain MHC class II binding ability.

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McCormick et al. do not teach a conjugate comprising the mutated superantigen and an antigen.

The '964 patent teaches that fusing a stable plasma protein to a protein ligand results in the enhanced in vivo plasma half life of the protein ligand (see column 5 in particular). The '964 patent teaches that the plasma protein is fused to the C-terminus of the protein ligand (see column 8 in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made fuse a stable plasma protein (i.e. a non-immunogenic antigen), as taught by the '964 patent, to the superantigen protein vaccine taught by McCormick et al. The ordinary artisan at the time the invention was made would have been motivated to do so, and have a reasonable expectation of success, since the '964 patent teaches that the fusion of stable plasma proteins enhances the in vivo plasma half life of a protein.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199


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(IN USA OR CANADA) or 571-272-1000.

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